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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/852,587	05/10/2001	Tahereh Tabatabaie	OKL010-105/00359A	8057

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EXAMINER	
SHAREH, SHAHNAM J	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 02/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/852,587	TABATABAIE ET AL.	
	Examiner	Art Unit	
	Shahnam Sharareh	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05/10/01, 11/10/2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *8,9 and 14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,10-13 and 15-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *05/01/01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-7, 10-13, 15-23 in Paper filed on Nov 06, 2003 is acknowledged. Applicant has failed to properly elect a species as recited in the Page 3 of the Election Requirement filed on October 03, 2003. Nevertheless, Examiner has withdrawn the species requirement to advance the prosecution.

This application contains claims 8-9, 14 drawn to an invention nonelected without traverse. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7, 10-13, 15-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of protecting progression of diabetes or treating insulin-dependent diabetes with a specific cyclooxygenase-2 inhibitor (Cox-2 inhibitors) such as NS-398 or a repressor of NF-kB activation such as PDTC, does not reasonably provide enablement for all cyclooxygenase 2-inhibitors or repressors of NF-kB activation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors that are to be considered in determining whether a disclosure would require undue experimentation are set forth *in In re Wands*, 858, F.2d 731, 736-40 (Fed. Cir. 1988). Accordingly, they include

1. The quantity of experimentation necessary
2. The amount of direction or guidance presented
3. The presence or absence of working examples
4. The nature of the invention
5. The state of the prior art
6. The relative skill of those in the art
7. The predictability or unpredictability of the art, and
8. The breadth of the claims.

The court has reasoned that "these factors are illustrative, not mandatory and what is relevant depends on the specific facts. All of these factors need not be reviewed when determining whether a disclosure is enabling." *Id.*

The instant claims merely call for a trial and error methodology that attempts to find a compound that reduce the risk of developing insulin-dependent diabetes in an individual having a possible predisposition or showing signs of development of Type I diabetes. The instant specification first fails to identify potential useful drugs or their mechanism of action for screening. Even though the specification may provide for an exemplary drug from the group of compounds known as Cox-2 inhibitors or NF-kB repressors, it does not provide necessary link between finding a particular compound or narrowing the range of candidates in order to find a suitable compound without the need

for undue experimentation. Particularly, it is not clear which Cox-2 inhibitor or repressor of NF-kB are able to reduce the risk of developing insulin-dependent diabetes.

Second, given the broad breadth of the claims the ordinary skill in the art would not have any guidance as what type of compounds should he proceed with to achieve the claimed intended purpose. Even though the level of ordinary skill in the art may allow practice of chemical assays to test compounds for a potential use, aside from NS-398 or PDTC and the short list in page 23-24, no where in the specification provides any guidance to select compounds that are likely to be of use in practicing the claimed invention consistent with the breath of the claims. Rather, the specification relies on hypothetical level of ordinary skill in the art to supply the missing information.

Further, as it has repeatedly been stressed by the Courts, a method for determining whether a given compound possesses certain desired characteristics and identifies some broad categories of compound that might work, without more precise guidelines, amount to little more that "a starting point, a direction for further research." See *Genetech v. Novo Nordisk A/S,* 108 F.3d 1361,1366,(Fed. Cir.), also *Enzo Biochem, Inc. V. Calgene*, Inc, 1888 F.3d 1362, 1374 (Fed. Cir. 1999), *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (CAFC 1997) at 1406. In the instant case, for example at page 23, specification asserts various types of potential candidates however, such compounds do not represent the entire class of Cox-2 inhibitors or repressors of NF-kB. Nor do they share a common structural feature. Thus, similar to the cases above, the instant claims appear to place a function at the point of novelty by identifying a compound that possesses certain desired characteristic. As has been

reasoned, such attempt does not satisfy the statutory requirement set forth under 112 1st para.

Finally, the instant claims are directed to "methods of prevention of insulin-dependent diabetes," without adequately providing evidence of this clinical outcome. At best as concluded in page 28 of the specification, the methodology appears to protect predisposed individuals against progression of diabetes. No where in the specification provided any guidance or working example as to "absolute prevention" of the condition.

Accordingly, the instant claims do not provide any guidance as to preventing insulin-dependent diabetes, nor does the specification provide for the entire genus of compounds employed for the claimed intended use. Further specification fails to provide notice for those practicing in the art about the limits of protection with respect to the compounds employed and the intended use. Rather, the claims simply appear to amount to "an invitation to experiment." Thus, practicing the entire scope of the instant claims require undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7, 10-13, 15-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "an individual having a possible predisposition to type I diabetes, is not defined in the specification and appears relative in nature. The specification does

not provide a standard for one of ordinary skill in the art to reasonably apprise the scope of the invention.

Claim 2 recites the limitation "the inhibition" or "the repression" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim Objections

Claims 1-7, 10-13, 15-23 are objected to because of the following informalities:

- The recitations of NS-398 and PDTC in the claims is ambiguous as there is no antecedent basis for such recitations.
- Further claim 10 calls for the use of "PTC" which appears to be a spelling error.
- Claim 2 appears incomplete.

Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5-7, 10-13, 15-18, 20, 22-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Clare-Salzer US Patent 5,939,069 (Clare-Salzer).

Clare-Salzer discloses methods of treating individuals at high risk of developing insulin-dependent diabetes (IDD) comprising administering NS-398. (col 5, lines 55-65; col 12, lines 34-44). Since Clare-Salzer meets all the elemental steps of the instant

claims, it also inherently provides for the mechanism of action by which Cox-2 asserts its effects. Thus, Clare-Salzer anticipates the limitations of instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-7, 10-13, 15-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Clare-Salzler in view of Bedoya et al (Biochemeical and Biophysical Research Communication, Vol 210, No. 3, 1995, pages 816-822) (Bedoya).

The teachings of Clare-Salzler are described above. Clare Salzler also teaches the use of an inhibitor of inducible nitric oxide synthase (iNOS) such as aminoguanidine with NS-398. (see col 5, lines 45-53, col 8, lines 50-col 9, line 40; col 12, lines 38-43). Clare-Salzler fails to specifically use PDTC.

Bedoya teaches that PDTC prevents the induction of iNOS in insulin-producing cells and calls for its use for treating early stage IDD. (see abstract, pages 819-821, specifically the conclusion of the article).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of invention to modify Clare-Salzler's method by substituting PDTC in place of aminoguanidine, because as suggested by Bedoya, the ordinary skill in the art would have had a reasonable expectation of success in preventing the induction of iNOS in insulin-producing celss and thus protecting these cells against destruction in the early stages of IDD.

Conclusion

No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 571-272-0630. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 703-308-1877. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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